REMARKS

Claims 52-75 are pending. Claims 21, 23, and 27-51 have been cancelled without prejudice or disclaimer as being drawn to a non-elected invention. Claims 1-20, 22, and 24-26 have also been cancelled without prejudice or disclaimer. New claims 52-75 have been added. New claims 52 and 67 are supported by claims 1 and 17 as originally filed, and by disclosure at page 18, lines 20-21 of the specification. New claim 53 is supported by claim 3 as originally filed. New claim 54 is supported by claim 6 as originally filed. New claims 55 and 56 are supported by disclosure at page 28, lines 14-17 of the specification. New claims 57 and 59 is supported by claims 1 and 17 as originally filed, page 28, lines 14-17 and page 26, lines 17-25 of the specification. New claim 58 is supported by claims 1 and 17 as originally filed, and page 28, lines 14-17. New claim 60 is supported by claim 19 as originally filed. New claim 61 is supported by claim 7 as originally filed. New claim 62 is supported by claim 8 as originally filed. New claim 63 is supported by claim 9 as originally filed. New claim 64 is supported by claim 10 as originally filed. New claim 65 is supported by claim 12 as originally filed. New claim 66 is supported by claim 13 as originally filed. New claim is supported by claim 14 as originally filed. New claim 69 are supported by claim 15 as originally filed. New claim 70 is supported by claim 16 as originally filed. New claims 71 and 73 are supported by claims 1 and 18 as originally filed. New claim 72 is supported by claim 19 as originally filed. New claim 73 is supported by claim 25 as originally filed. New claim 74 is supported by claim 25 as originally filed. New claim 75 is supported by claim 26 as originally filed. No new matter has been added by this amendment.

Support for the abstract inserted after the claims can be found throughout the specification, and also on the front page of PCT/US00/03592, from which the instant application is a 35 U.S.C. § 371 filing. No new matter is added.

Priority

The Examiner asserted on page 2, section 2 of the Office Action that a specific reference to any non-provisional application must include the relationship between the applications. Applicants have herein amended the specific reference found in the first sentence of the application to specify that the instant application is a 35 U.S.C. § 371 entry of PCT/US00/03592 filed February 11, 2000 which, claims priority to United States provisional patent application 60/119,725, filed February 12, 1999; and is a continuation-in-part of United States utility patent application 09/422,844, filed October 21, 1999, which claims priority to United States provisional patent application 60/168,407, filed December 1, 1999. Thus, Applicants contend that the instant specification, as presently amended, complies with 37 CFR §§ 1.78(a)(2) and (a)(5).

Specification

The Examiner also asserted on page 2, section 3 of the Office Action that an abstract of the disclosure as required by 37 CFR § 1.72(b) on a separate sheet is required. Applicants have herein amended the specification to include the abstract on a separate sheet after the claims.

Information Disclosure Statement

The Examiner asserted on page 3, section 4 of the Office Action that the information disclosure statement filed on October 11, 2002 does not completely comply with the provisions of 37 CFR §§ 1.97, 1.98 and MPEP § 609. Applicants submit, herewith, an IDS which supplies the missing elements of the references cited on the IDS filed on October 11, 2002. The appropriate fee under 37 C.F.R. § 1.17(p) is also submitted.

Double Patenting

The Examiner has also rejected claims 1, 2, 5, 7-10, 13, 16, 20 and 25 under 35 U.S.C. § 101 for statutory type double patenting in light of U.S. Patent No. 6,468,794, (the "'794 patent"). (*See* Office Action at pages 3-4). Applicants have canceled all of these claims, so the rejection, insofar as it pertains to these claims, is moot. Applicants traverse this rejection in the context of the claims presently added by the Applicants.

A rejection based on statutory type double patenting is only proper when the claims rejected are drawn to identical subject matter of the prior art. (*See Miller v. Eagle Mfg. Co.,* 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970)). New claims 52-75 each include the step of selecting

and eliminating from the population those cells that bind to a second antibody, wherein that antibody binds to CD45 antigen, or CD34 antigen, or both antibodies, or the step of selecting and eliminating from the population those cells that are $CD45^+$, $CD34^+$ or $CD45^+CD34^+$. The claims of the '794 patent do not include these steps. Thus, Applicants have added new claims that are not coextensive in scope with the claims of the '794 patent. As such, the invention claimed in the '794 patent is not drawn to the same subject matter as the pending claims. Therefore, Applicants submit that this rejection has been overcome.

The Examiner has also rejected claims 3, 4, 6, 11-12, 14-15, 17-19, 22, 24 and 26 under the judicially created doctrine of obviousness-type double patenting, in light of claims 1-13 of the '794 patent. (*See* Office Action at page 4). Applicants have canceled these claims, so the rejection is now moot as it applies to these claims. Moreover, for the reasons articulated above, Applicants assert that new claims 52-75 are not obvious in view of claims 1-13 of the '794 patent. Therefore, these new claims should not be rejected under the judicially created doctrine of obviousness-type double patenting.

Claim Objections

The Examiner has objected to claims 3-4 and 6 as being in improper dependent form for failing to further limit the subject matter of the previous claim. (*See* Office Action at page 5). Applicants have herein canceled claims 3-4 and 6, thereby rendering this objection moot. Moreover, Applicants assert that this objection does not apply to new claims 52-75.

Claim Rejections

Rejections under 35 USC § 112

The Examiner has rejected claims 1-20, 22 and 24-26 under 35 U.S.C. § 112, first paragraph, for lack of enablement. (*See* Office Action at page 5). Applicants have canceled claims 1-20, 22 and 24-26, so this rejection, as it applies to these claims, is moot. Moreover, Applicants contend that this rejection is not applicable to presently added claims 52-75.

Claims 52, 57, 58, 59, and 73 are drawn to methods of producing populations highly enriched for human central nervous system stem cells, by selecting a population that binds to monoclonal antibodies AC133 and/or 5E12, and eliminating from the population those cells that bind to a second antibody, such as a monoclonal antibody that binds to CD34 and/or CD45. Applicants submit that claims 52, 57, 58, 59, and 73, as well as all claims directly or indirectly depending from these claims, are enabled in light of the Examiner's above mentioned rejection.

The Examiner indicated in the Office Action on page 5, first paragraph of section 8, that the specification is enabling for, "a method of producing a population of highly enriched populations of human CNS stem cells using identifiable/deposited antibodies." Claims 52, 57, 58, 59, and 73 all specify that monoclonal antibodies AC133 and/or 5E12 must be used, and these antibodies are identifiable and have have been deposited with the American Type Culture Collection. Thus, Applicants contend that these claims, to the extent that they recite methods of producing of highly enriched populations of human CNS stem cells using monoclonal antibodies AC133 and/or 5E12, are enabled by the specification.

The Examiner also indicated, on page 5, paragraph 8 of the Office Action, that rejected claims 1-20, 22 and 24-26 did not reasonably provide enablement for methods of isolating highly enriched populations of human CNS stem cells using unknown or uncharacterized antibodies toward unknown determinants on the surface of cells. According to the Examiner, "[D]etection/recognition by structurally uncharacterized antibodies encompass random modifications or mutations or truncations of 'determinants on a cell surface', which would be expected by the skilled artisan to result in the use of antibodies that cross-react with different proteins, or in the use of antibodies that do not recognize the desired epitopes unique to neural stem cells." (Office Action at pg. 6, second paragraph). Applicants submit that, in light of these statements by the Examiner, the steps specified in new claims 52, 57, 58, 59 and 73 (and their respective dependent claims, which encompass eliminating from the population those cells that bind to a second antibody, such as a monoclonal antibody that binds to CD34 or CD45, are enabled by the specification.

First, a monoclonal antibody which binds to CD34 or CD45, two known surface expressed polypeptides, would not require the use of an uncharacterized antibody toward an unknown determinant on the cell, as these antibodies are characterized by the ability to bind to CD34 or to CD45. Moreover, as indicated in the instant specification, antibodies to CD34 and CD45 are commercially available. (*See* page 8, lines 25-32 of the specification). Thus, Applicants contend that, contrary to the Examiner's assertion, monoclonal antibodies that bind to CD34 or CD45 are characterized antibodies that bind to known determinants.

Second, the identification (and use) of antibodies characterized by their ability to bind to CD34 and CD45 could be accomplished by the skilled artisan without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. (*See In re Wands* 585 F.2d 731, 737).

In the instant specification, Applicants have provided a working example that demonstrates a method for isolating highly enriched populations of human CNS stem cells, using commercially acquired CD34 and CD45 antibodies, to eliminate a fraction of cells which bound these antibodies. (*See* Example 3, especially, page 18, lines 18-30 of the instant specification). Further, Applicants have also provided another working example which demonstrates a method for isolating highly enriched populations of human CNS stem cells, using commercially acquired CD34 and CD45 antibodies using fluorescence activated cell sorting. (*See* Example 10, especially page 26, lines 27-29, and page 28, lines 17-22 of the instant specification). Thus, Applicants note that, the instant specification provides ample guidance (including several working examples) regarding how to practice the claimed methods.

Thus, based on the teachings of the instant specification, Applicants contend that those skilled in the art would recognize that any antibody that binds to CD34 or to CD45 could be used in the claimed methods. Moreover, it would require only a minimal amount of experimentation to ascertain whether an antibody that binds to CD34 or CD45 would work. By comparing the results obtained in the specification with the results obtained using different antibodies that bind to CD34 or to CD45, one skilled in the art would be able to practice the claimed invention without undue experimentation.

Moreover, the nature of the claimed invention concerns the further enrichment of central nervous system stem cells by selecting and eliminating those cells that do not express the CD34 and/or CD45 antigens on their cell surface. These antigens (as well as antibodies specific to them) are known in the prior art. Thus, one of ordinary skill in the art would predict that antibodies that bind specifically to CD34 or CD45 would have a high probability of working in the claimed methods.

Therefore, for all of these reasons, Applicants believe that new claims 52, 57, 58, 59, and 73 (as well as dependent claims 53-56, 60-70 and 74-75) are fully enabled by the as-filed specification.

Applicants also note that new claim 71 and new claim 72, which depends from claim 71 are also enabled in light of the Examiner's statements in the Office Action. Claim 71 is drawn to a method of isolating a population of cells enriched for human central nervous system stem cells which can initiate neurospheres by selecting cells that are $AC133^+$, $5E12^+$, or $AC133^+5E12^+$, and by eliminating cells that are $CD45^+$, $CD34^+$, or $CD45^+CD34^+$. As explained above, specific methods and working examples are provided in the instant specification to carry out such methods. Thus, one of ordinary skill in the art, with the instant specification in hand, would be able perform the claimed methods without undue experimentation. Therefore, Applicants submit that new claims 71 and 72 are also enabled by the as-filed specification.

Therefore, Applicants submit that new claims 52-75 are fully enabled. Thus, this rejection does not apply to these new claims.

The Examiner has also rejected claims 1-20, 22, and 24-26 under 35 U.S.C. § 112, second paragraph for being indefinite for reciting the term "reagent". Claims 1-20, 22, and 24-26 have been canceled, so this rejection is moot as it applies to these claims. Moreover, this rejection does not apply to the new claims, as none of these claims recite this limitation.

The Examiner has also rejected claims 24-26 under 35 U.S.C. § 112, second paragraph for being indefinite for reciting the phrase, "one or more predetermined growth factors effective..." and, "neural survival factor (NSF)". Claims 24-26 have been canceled, so this rejection is moot as it applies to these claims. Moreover, none of the new claims recite the phrase, "one or more predetermined growth factors effective..." Thus, this rejecton does not apply to new claims 52-75.

Likewise, contrary to the Examiner's contention, the phrase "neural survival factor (NSF)" is definite. This phrase is defined in the specification on page 19, line 18, which indicates that NSF can be purchased from Clonetics in San Diego, CA (Cat. CC-4323). Thus, Applicants note that neural survival factor is a specific and defined cytokine. Therefore, the recitation of this term in new claim 75 does not render this claim indefinite. Thus, Applicants submit that this rejection does not apply to new claims 52-75.

The Examiner has also rejected claims 17-20, 22 and 24-26 under 35 U.S.C. § 112, second paragraph for being indefinite for being ambiguous and contradictory in stating, "select... for reduced contact" based on "binding" to a CD45 or CD34 antigen. The Examiner has also rejected these claims for reciting the "lo" phenotype. As claims 17-20, 22 and 24-26 have been canceled herein, this rejection is moot as it applies to these claims. Moreover, this rejection does not apply to new claims 52-75. The presently added claims recite, "selecting and eliminating from the population those cells that bind to a second antibody selected from the group consisting of a monoclonal antibody that binds to CD45 antigen and a monoclonal antibody that binds to CD34 antigen." Applicants contend that this limitation is neither ambiguous or contradictory. Thus, this rejection does not apply to new claims 52-75.

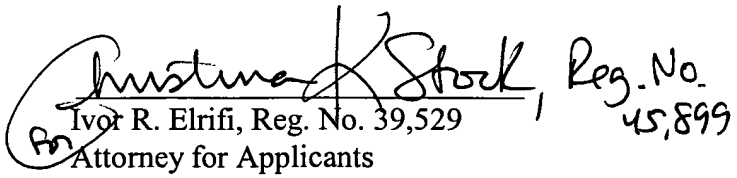
Likewise, none of the new claims recite the "lo" phenotype. Therefore, Applicants submit that this rejection also does not apply to new claims 52-75.

CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Dated: September 7, 2004



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